

“THE ONE-SEX MIXING PROBLEM: A CHOICE OF SOLUTIONS?”

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Abstract

The problem of who is sexually mixing with whom is of critical importance in determining the transmission dynamics of HIV/AIDS. Several solutions, or mixing functions, that satisfy natural mixing constraints have been proposed over the last few years. In this article we present a formula describing the general solution to the mixing problem and explicitly show that the mixing structures found in the literature are special cases. This formula reduces the problem of choosing a mixing structure to that of estimating the relevant mixing parameters.

The transmission dynamics of HIV/AIDS, and of sexually transmitted diseases (STDs) in general, is highly dependent on the population social/sexual mixing structure, i.e., how many partners and who they are. STD epidemic models require mathematical descriptions of mixing which must satisfy various natural constraints. A few such solutions to the one-sex (homosexual) mixing problem have been found, and there has been some confusion as to which is the "correct" one to use. Only one of the solutions is completely general, however, and is sufficiently straightforward to apply that its use as a standard is suggested as it also reduces the problem of choosing a mixing function to that of estimating parameters.

The development of predictive models of the transmission dynamics of HIV, gonorrhea, syphilis, etc. has been severely hampered by the lack of a mathematical framework allowing a realistic description of social/sexual mixing. This is true both of one-sex (homosexual) and two-sex (heterosexual) epidemics. The problem has been discussed in detail in the literature (1,2) and arises because descriptions of mixing (who everyone's partners are) are specified only by a set of constraints (1-4). In a one-sex population with N distinct groups, if $p_{ij}(t)$ is the mixing function (fraction of partners taken by people in group i among those in group j at time t), then the constraints amount to making the $\{p_{ij}(t)\}$ a set of probabilities, conserving the number of partnerships between each pair of groups, and ensuring that no one can take partners from an empty group. As N discrete groups are usually more convenient for practical modeling purposes than a continuum description, we shall use the former throughout, noting only that all results can easily be extended to the continuum case.

To date four solutions $p_{ij}(t)$ to the one-sex mixing problem have been found (Table I). The earliest, best known and most widely used is ((A) in Table I) proportionate or random mixing (8-11), where mixing among groups occurs in proportion to the total number of partnerships formed by all the people in each group. Although easy to apply, (A) suffers from the disadvantage that human mixing behavior is not believed to be random. For this reason other solutions were sought.

In "preferred mixing" ((B) in Table I), the $p_{ij}(t)$ are formed by having the members of each group always reserve a constant fraction of its partners among themselves, the rest being spread randomly over all groups (10-12). Hyman and Stanley's (13) mixing function ((C) in Table I) is a much more general form of $p_{ij}(t)$, involving an arbitrary function of i and j (in our notation, it was originally formulated in the continuum case).

The fourth solution, generalized mixing, (3,7) (D in Table I), includes like-with-like mixing ($\phi_{ij} = \phi(|i-j|)$, e.g. $\phi_{ij} = \alpha e^{-\theta(i-j)^2}$, (1,13)). It can be shown (3,7) that (D) is a true general solution, with *all* possible solutions expressible in this form, i.e., multiplicative perturbations of random (proportionate) mixing. The key to the general solution is the set of (possibly time-dependent) parameters $\{\phi_{ij}\}$. These must be chosen such that none of the functions $\{R_i(t)\}$ (see Table I) are

negative. If the $\{\phi_{ij}\}$ are constants, then because they prescribe the multiplicative perturbation, they describe a time-variant deviation from random mixing (a rough measure (14) of this deviation is the simple range $e = \phi_{\max} - \phi_{\min}$). If the $\{\phi_{ij}\}$ vary with time, then they represent the time-dependent variation from random mixing.

Demonstrating that the other solutions are special cases of the General Solution (D) involves finding a set of $\{\phi_{ij}\}$ that recovers them. The third column in Table I lists appropriate $\{\phi_{ij}\}$ for the various solutions. Note that as the relationship is non-unique (14), there exist many distinct sets of $\{\phi_{ij}\}$, which will recover any particular solution. This is particularly clear for proportionate mixing. Note also that the equivalent $\{\phi_{ij}\}$ for "preferred mixing" (B) are time-dependent. Hence the distance from random mixing in this case varies with time (not surprising as the reserved fractions do not depend on group population sizes).

It should also be clear that Hyman and Stanley's (13) solution (C) is not another form of the General Solution, being a broad but nonetheless special case: there clearly exist a great many allowable $\{\phi_{ij}(t)\}$ for which the $\{F_{ij}\}$ of Table I (C) cannot be time-independent (including those prescribing preferred mixing (B)). Further, we would not expect there to be many constant ϕ_{ij} cases where the F_{ij} are also constant (except for proportionate mixing itself), so that (C) shares a feature with (B), namely time-variable distance from proportionate mixing.

We note in passing that the empirical approach of Gupta et al. (17), where the $\{p_{ij}(t)\}$ are held constant at their initial ($t=0$) values by judiciously altering the group activity levels ($\{c_i(t)\}$ in Table I), does maintain a constant distance from proportionate mixing, but only at the cost of altering the proportionate mixing functions ($\{\bar{p}_i(t)\}$ in Table I) themselves through their assumption of adaptive sexual behavior change.

The other formal solutions are restrictive special cases of the General Solution, and they have the (we think disadvantageous) feature of implying a variable (artificially imposed) distance from random mixing. Further, estimation of the $\{\phi_{ij}\}$ is in principle feasible (14-16) most valuably if they can, in fact, be assumed constant. We would argue that any selection of a particular solution must be justified in each case, and that the most appropriate approach is to start with the general solution (D) and see if simplification is possible, on the basis of comparison with sampled sexual activity data.

Given these arguments, and the observation that a similar general solution has been obtained for mixing in heterosexual populations (4,23) (uniting the classical (11) and pair-formation (5) formalisms), we would suggest that (D) be adopted as the standard in one-sex multiple group heterogeneous activity STD epidemic modelling. Approaches that allow for spatially dependent mixing behavior have begun to be developed through judicious reinterpretations of the social/nonsocial framework of Sattenspiel (18-22).

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Table I
Relationship Between Mixing Functions

Mixing function	$p_{ij}(t)$	$\phi_{ij}(t)$
(A) Proportionate mixing ^a	$\bar{p}_j(t) \equiv \frac{c_j(t)T_j(t)}{\sum_{k=1}^n c_k(t)T_k(t)}$	$\alpha, \text{ all } i, j$ $0 \leq \alpha < 1$
(B) Deferred mixing ^b	$\delta_{ij}f_i + (1-f_i) \frac{(1-f_j)\bar{p}_j(t)}{\sum_{k=1}^n (1-f_k)\bar{p}_k(t)}$	$\delta_{ij}f_i / \bar{p}_i(t)$
(C) Stanley's function ^c	$\left[1 - \sum_{k=1}^i p_{ik}(t) \right] \frac{F_{ij}\bar{p}_j(t)}{\sum_{k=1}^i F_{ik}\bar{p}_k(t)}, \quad j > i$ $p_{ji}(t)\bar{p}_j(t) / \bar{p}_i(t), \quad j < i$	Any solution of $F_{ij} = R_i(t)R_j(t) + \phi_{ij}(t) \sum_{k=1}^n R_k(t)\bar{p}_k(t)$ where $R_i(t) = 1 - \sum_{k=1}^n \bar{p}_k(t)\phi_{ik}(t)$
(D) General solution	$\bar{p}_j \left[\frac{R_i(t)R_j(t)}{\sum_{k=1}^n \bar{p}_k(t)R_k(t)} + \phi_{ij}(t) \right]$	Any $\phi_{ij}(t)$ such that $R_i(t) \geq 0$, all i and t , at least one $R_i(t) > 0$, $\phi_{ij}(t) = \phi_{ji}(t)$, all i, j, t .

Particular solutions (A-C) and the general solution (D) to the N-group one-sex mixing problem. The $\{p_{ij}(t)\}$ is the mixing matrix or function itself (explanation in text), and $\phi_{ij}(t)$ are parameters used in the General Solution to recover the particular solutions.

^a $c_i(t)$ and $T_i(t)$ are respectively the number of new partners taken by an individual per unit time and the total population of group i .

^b $\delta_{ij} = 1$ if $i = j$, zero elsewhere

^c originally formulated in continuous case